

*Table S1 – Tumor line generation classifications, related to Figure 2*

<b>Classifier</b>	<b>Generations</b>
Early	Parental, LN1, LN2
Mid	LN3, LN4, LN5
Mid-Late	LN6
Late	LN7, LN8, LN9

*Table S2 – Sample groupings for DGE Analysis, related to Figure 2*

<b>Early vs. Late</b>	
B16-F0	LN7-1112AR
LN1-15IL	LN7-1120BL
LN1-16IL	LN7-1134BL
LN1-18IL	LN8-1205BL
LN1-24IR	LN8-1194BR
LN2-189ILR	LN8-1198AR
LN2-225IR	LN9-1315BL
LN2-262IL	LN9-1358IR
<b>Parental vs. LN8</b>	
B16-F0	LN8-1205BL
	LN8-1194BR
	LN8-1198AR
<b>Parental vs. LN1</b>	
B16-F0	LN1-15IL
	LN1-16IL
	LN1-18IL
	LN1-24IR
<b>Phy1 vs. Rest</b>	
LN1-15IL	LN1-16IL
LN2-189ILR	LN1-18IL
LN3-384IR	LN1-24IR
LN4-473BL	LN2-225IR
LN5-809CL	LN2-262IL
LN6-987AL	LN3-392AL
LN6-880AL	LN3-377IR
LN7-1134BL	LN4-533BL
LN8-1198AR	LN4-521BL
LN9-1358IR	LN5-712AL
	LN5-716BR
	LN6-877AL
	LN6-944AL
	LN6-991AL
	LN7-1112AR

	LN7-1120BL
	LN8-1205BL
	LN8-1194BR
	LN9-1315BL
<b>Phy2 vs. Rest</b>	
LN1-16IL	LN1-15IL
LN2-262IL	LN1-18IL
LN3-392AL	LN1-24IR
LN4-533BL	LN2-189ILR
LN5-716BR	LN2-225IR
LN6-991AL	LN3-377IR
LN7-1112AR	LN3-384IR
LN8-1205BL	LN4-473BL
LN8-1194BR	LN4-521BL
LN9-1315BL	LN5-712AL
	LN5-809CL
	LN6-877AL
	LN6-944AL
	LN6-987AL
	LN6-880AL
	LN7-1120BL
	LN7-1134BL
	LN8-1198AR
	LN9-1358IR
<b>Phy3 vs. Rest</b>	
LN1-18IL	LN1-15IL
LN3-377IR	LN1-16IL
LN4-521BL	LN1-24IR
LN5-712AL	LN2-189ILR
LN6-877AL	LN2-225IR
LN7-1120BL	LN2-262IL
	LN3-392AL
	LN3-384IR
	LN4-473BL
	LN4-533BL
	LN5-716BR
	LN5-809CL
	LN6-944AL
	LN6-987AL
	LN6-880AL
	LN6-991AL
	LN7-1112AR
	LN7-1134BL
	LN8-1205BL
	LN8-1194BR

	LN8-1198AR
	LN9-1315BL
	LN9-1358IR

*Table S3 – IDs of Patient HNSCC RNA-seq Samples used for Analysis, related to Figures 2 and 4*

<b>RNA-seq sample ID</b>	<b>Sample type</b>
7175_T	primary N0
7177_T	primary N0
7184_T	primary N0
7207_e_T	primary N0
7176_T	primary N+
7174_T	primary N+
7195_T	primary N+
7197_T	primary N+
7202c_T	primary N+
7202_T	primary N+
7204_T	primary N+
7205_Col_T	primary N+
7205_T	primary N+
7211_T	primary N+

*Table S4 – Oligonucleotides, related to STAR Methods*

<b>Name</b>	<b>Oligo Type</b>	<b>Sequence (5' -&gt; 3')</b>
Cd274 CDS PCR1 F	Primer	GCCACCATGAGGATATTGCTGGCATTATATTG
Cd274 CDS PCR1 R	Primer	CGGGAATTCTTACGTCTCCTCGAATTGTGTATC
Cd274 CDS PCR2 F	Primer	ATTACTAGTGCCGCCACCATGAGGATATTGCTGC
Cd274 CDS PCR2 R	Primer	TCTAGACCCGGGAATTCTTACGTCTCCTCG
sgCntrl	sgRNA	GTATGGCAGCAACGTCACGA
sgCntrl	sgRNA	TGCGAATACGCCACGCGAT
sgCd274-1	sgRNA	GCCTGCTGTCACTTGCTACG
sgCd274-5	sgRNA	CTTGACGTCTGTGATCTGAA
sgB2m-4	sgRNA	AGTATACTCACGCCACCCAC
sgB2m-6	sgRNA	TCGGCTTCCCATTCTCCGGT
sglfnar1	sgRNA	GGCGCGGCGGCCCTGGTGC
sglfngr1	sgRNA	GTCCTGATGCTGTCTGCGA
sgStat1-1	sgRNA	GGATAGACGCCAGCCACTG
sgStat1-3	sgRNA	TTAATGACGAGCTCGTGGAG
sglfnb-3	sgRNA	GCTGCTTATAGTTGATGGAG
sglfnb-4	sgRNA	GACGAACATTGGAAATGTC